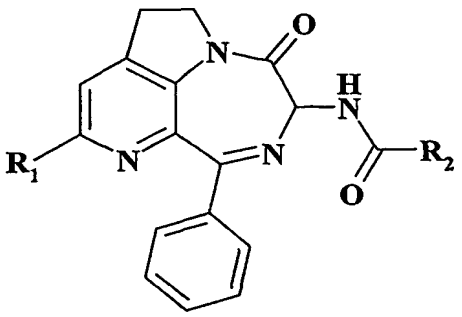
CLAIMS

1- Compounds of formula (I):



(I)

characterized in that:

- R_1 represents a group selected from hydrogen atom, methyl, methoxy, hydroxy, amino, dimethylamino, acetamido, pyrrolidin-1-yl, and hydroxymethyl;
- R_2 represent a group selected from phenyl, pyridyl, pyrimidyl, quinolyl, isoquinolyl, indolyl, pyrolyl, [1,2,3]-triazolyl, benzo[c]isoxazolyl, thienyl, pyrazolyl, isothiazolyl, imidazolyl, benzofuranyl, pyrazolo[5,1-*c*][1,2,4]triazyl each of these groups being optionally substituted from 1 to 3 groups, identical or different independently of each other, selected from halogen, trifluoromethyl, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, hydroxy, amino, acetamido, tert-butyloxycarbonylamino, cycloalkylcarbonylamino, sulfonamide, nitro, acetylmethoxy, cyclopentyloxy;

and optionally, their optical isomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

2- Compounds of formula (I) according to claim 1 characterized in that:

- R_1 represents a group selected from methyl, methoxy, amino and acetamido;
- R_2 represents a group selected from phenyl, pyridin-3-yl, and pyridin-4-yl, each of these groups being optionally substituted from 1 to 3 groups, identical or different independently of each other selected from halogen, methoxy and amino;

and optionally, their optical isomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

3- Compounds of formula (I) according to anyone of claims 1 or 2 characterized in that R_2 represents a pyridin-4-yl or a pyridin-3-yl group optionally substituted from 1 to 3 groups as defined in claim 1, and optionally, their optical isomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

4- Compounds of formula (I) according to anyone of claims 1 or 2 characterized in that R_1 represents a group selected from methoxy and amino, and R_2 represents a pyridin-3-yl, and optionally, their optical isomers, and addition salts thereof with a pharmaceutically acceptable acid or base.

5- A compound of formula (I) according to claim 1, which is:

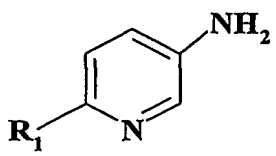
- *N*-(4-methoxy-9-oxo-6-phenyl-1,2,8,9-tetrahydro-5,7,9a-triaza-benzo[*cd*]azulen-8-yl)-nicotinamide,

its optical isomers, and addition salt thereof with a pharmaceutically acceptable acid or base.

6- A compound of formula (I) according to claim 1, which is the (1R) *N*-(4-methoxy-9-oxo-6-phenyl-1,2,8,9-tetrahydro-5,7,9a-triaza-benzo[*cd*]azulen-8-yl)-nicotinamide, and addition salt thereof with a pharmaceutically acceptable acid or base.

7- A compound of formula (I) according to claim 1, which is the (1S) *N*-(4-methoxy-9-oxo-6-phenyl-1,2,8,9-tetrahydro-5,7,9a-triaza-benzo[*cd*]azulen-8-yl)-nicotinamide, and addition salt thereof with a pharmaceutically acceptable acid or base.

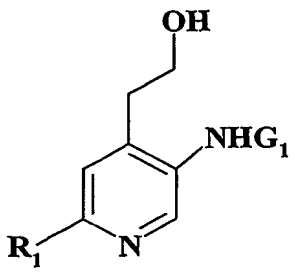
8- A process for the preparation of the compound of formula (I) characterized in that there is used as starting material a compound of formula (II):



(II)

in which R_1 is as defined in the compound of general formula (I),

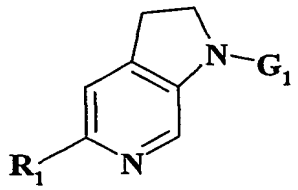
compound of formula (II) in which the primary amino group is protected in a first step by a usual protective group (G_1) used classically in organic synthesis, then is treated with oxirane or bromoethanol, in presence of a strong base to yield the compound of formula (III):



(III)

in which R_1 and G_1 are as defined hereinbefore,

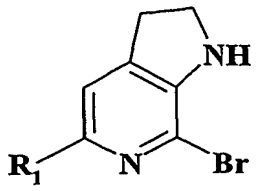
compound of formula (III) which is reacted with methanesulfonyl chloride to yield the corresponding mesylate intermediate (in the place of the primary alcohol), which is treated directly in polar condition with LiHMDS to yield to the cyclized compound of formula (IV):



(IV)

in which R_1 and G_1 are as defined hereinbefore,

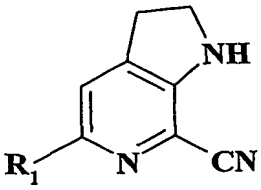
compound of formula (IV) which is treated with hydrogen bromide in the presence of hydrogen peroxide to yield to the corresponding 7-bromo-pyrrolo[2,3-*c*]pyridin of formula (V):



(V)

in which R_1 is as defined hereinbefore,

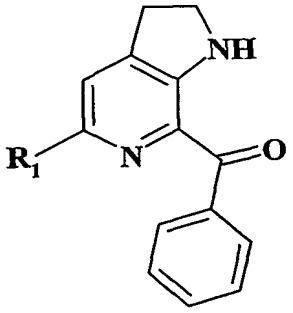
compound of formula (V), which is reacted with zinc cyanide under palladium condition or with cupper cyanide under heating or micro-wave conditions to yield to the corresponding cyanide compound of formula (VI):



(VI)

in which R_1 is as defined hereinbefore,

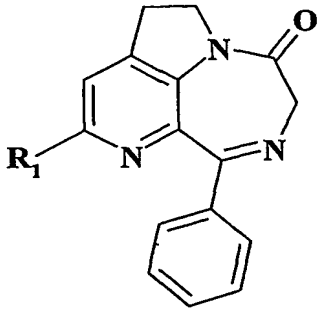
which compound of formula (VI) being treated with phenylmagnesium bromide under polar solvent to yield to the compound of formula (VII):



(VII)

in which R_1 is as defined hereinbefore,

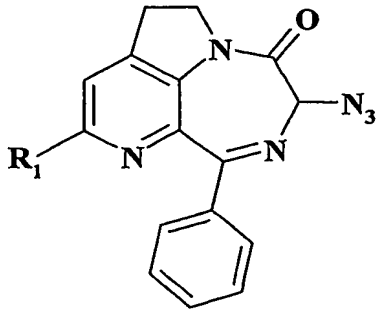
compound of formula (VII) being condensed with methyl glycinate hydrochloride in presence of pyridine, to yield to the compound of formula (VIII):



(VIII)

in which R_1 is as defined hereinbefore,

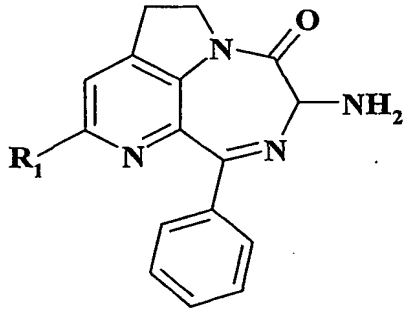
which compound of formula (VIII) is reacted with trisylazide to yield to the compound of formula (IX):



(IX)

in which R_1 is as defined hereinbefore,

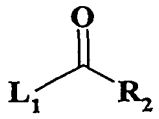
compound of formula (IX) being reduced under smooth conditions with triphenylphosphine in wet tetrahydrofurane to yield to the amino derivative of formula (X):



(X)

in which R_1 is as defined hereinbefore,

which compound of formula (X) being reacted under peptidic coupling conditions in basic medium using a classical coupling agent of organic synthesis with a compound of formula (XI):



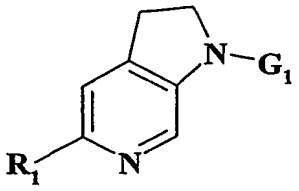
(XI)

in which R_2 is as defined in the compounds of general formula (I) and L_1 represent a leaving group like halogen or (C_1-C_4)alkoxy,

to yield to the compound of formula (I), which are purified, where appropriate, according to a conventional purification technique, which are separated, where appropriate, into their different isomers according to a conventional separation technique, and which are

converted, where appropriate, into addition salts thereof with a pharmaceutically-acceptable acid or base.

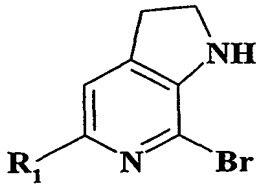
9- Intermediate compounds of formula (IV):



(IV)

in which R_1 is as defined in the compound of formula (I) in claim 1, and G_1 represents a protecting group of the amino group classically used in organic synthesis, except that (IV) does not represent 1-(2,3-dihydro-pyrrolo[2,3-*c*]pyridin-1-yl)acetate and *tert*-butyl 1-(2,3-dihydro-pyrrolo[2,3-*c*]pyridin-1-yl)carboxylate.

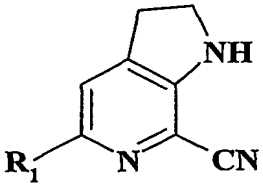
10- Intermediate compounds of formula (V):



(V)

in which R_1 is as defined in the compound of formula (I) in claim 1.

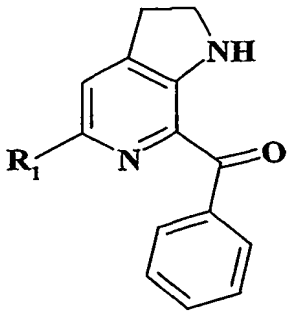
11- Intermediate compounds of formula (VI):



(VI)

in which R_1 is as defined in the compound of formula (I) in claim 1.

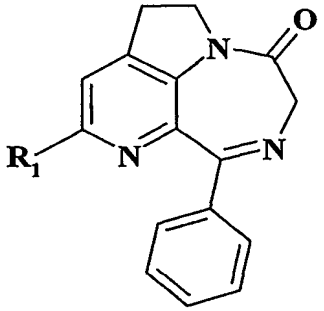
12- Intermediate compounds of formula (VII):



(VII)

in which R_1 is as defined in the compound of formula (I) in claim 1.

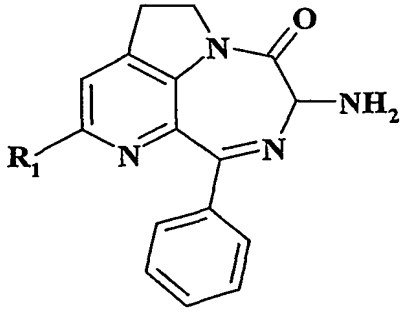
13- Intermediate compounds of formula (VIII):



(VIII)

in which R_1 is as defined in the compound of formula (I) in claim 1.

14- Intermediate compounds of formula (X):



(X)

in which R_1 is as defined in the compound of formula (I) in claim 1.

15- A method for treating a living body afflicted with a disease where the inhibition of phosphodiesterase type 4 is involved, comprising the step of administering to the living body an amount of a compound of claim 1 which is effective for alleviation of said conditions.

16- A method for treating a living body afflicted with a disease selected from cancer, acquired immunodeficiency syndrome, fibrosis, excessive scarring including excessive dermal scarring such as normal or abnormal dermal scarring following wounding or surgery, osteoarthritis, osteoporosis, multiple sclerosis, anxiety, depression, atopic dermatitis, rheumatoid arthritis, septic shock, immune diseases including disseminated lupus erythematous, psoriasis, graft rejection and allergic rhinitis, as well as diseases involving the production of TNFα, inflammatory complaints such as asthma, chronic obstructive bronchopneumopathy (COPD), post-ischaemic lesions, pulmonary hypertension, congestive cardiac insufficiency, acute respiratory distress syndrome, and chronic inflammatory diseases of the intestine (IBD) such as Crohn's disease and ulcerative colitis, comprising the step of administering to the living body an amount of a compound of claim 1 which is effective for alleviation of said conditions.

17- A pharmaceutical composition comprising as active ingredient an effective amount of a compound as claimed in claim 1, alone or in combination with one or more pharmaceutically-acceptable excipients or carriers.

18- A pharmaceutical composition useful in the method of Claim 15 comprising as active ingredient an effective amount of a compound as claimed in claim 1, together with one or more pharmaceutically-acceptable excipients or carriers.

19- Use of a compound according to Claim 1, for the preparation of a medicinal product intended for treating a disease involving therapy by inhibition of type 4 phosphodiesterase.

20- Use according to Claim 19, characterized in that the disease is cancer, acquired immunodeficiency syndrome, fibrosis, excessive scarring including excessive dermal scarring such as normal or abnormal dermal scarring following wounding or surgery, osteoarthritis, osteoporosis, multiple sclerosis, anxiety, depression, atopic dermatitis, rheumatoid arthritis, septic shock, immune diseases including disseminated lupus erythematous, psoriasis, graft rejection and allergic rhinitis, as well as diseases involving the production of TNFα, inflammatory complaints such as asthma, chronic obstructive

bronchopneumopathy (COPD), post-ischaemic lesions, pulmonary hypertension, congestive cardiac insufficiency, acute respiratory distress syndrome, and chronic inflammatory diseases of the intestine (IBD) such as Crohn's disease and ulcerative colitis.

21- Use according to Claim 19, characterized in that the disease is selected from chronic obstructive bronchopneumopathy, asthma and chronic inflammatory diseases of the intestine (IBD) such as Crohn's disease and ulcerative colitis.

22- Use according to Claim 19, characterized in that the disease is selected from chronic obstructive bronchopneumopathy and asthma.